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TITLE: Integrative Analysis of Genome-wide Gene Expression for Prostate Cancer Prognosis

PRINCIPAL INVESTIGATOR: Jiyoung Ahn, Ph.D.

CONTRACTING ORGANIZATION: New York University
New York, NY 10016

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Jiyoung Ahn

E-Mail: jiyoung.ahn@nyumc.org

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14. ABSTRACT

We aim to examine the association of genome-wide mRNA transcription profiles in prostate tumor tissue with PSA recurrence and systemic progression (metastasis), in a consortium study based on Mayo and NYU prostate cancer cohorts. We have completed research steps as planned in Mayo cohort, but we have a 5-6 month unexpected delay in NYU samples. PI gave an invited talk at a cancer center based on the concept of this study under the DOD funding.

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INTRODUCTION

The specific aims of the project have not changed. Using the resources from the Mayo and NYU cohorts, we are conducting:

Aim 1. Examine the association of genome-wide mRNA transcription profiles in prostate tumor tissue with PSA recurrence in men who had prostate cancer. We will compare gene expression profile between 400 PSA recurrent men (defined as a follow-up PSA > = 0.20 ng/ml) and 400 non PSA recurrent men.

Aim 2. Examine the association of genome-wide mRNA transcription profiles in prostate tumor tissue with systemic progression in men who had a biochemical (PSA) recurrence of prostate cancer. We will compare gene expression profile between 200 systemic progressors (defined as a positive bone scan or CT scan with 5 years of PSA recurrence) and 200 non-progressors, who remained negative for at least 5 years.

Our underlying hypothesis is that mRNA transcription profile plays an important role in shaping phenotypic inter-individual differences in tumor behavior related to prostate cancer prognosis. The ultimate goal of this study is to identify biomarkers that can be used at the time of diagnosis to predict risk of recurrence and improve clinical treatment decision making.

This study is being conducted over 2 years with the timeline shown in the table below**.** Note that the time sequence of tasks is not necessary the sequence of the study Aims.

BODY:

We have addressed our study progress by planned task in year 1.

Task 1. **Study population selection (Months 1-2):**

Selecting nested case-control study population in NYU cohort
Selecting nested cases-control study population in Mayo cohort

1. Completed nested case control selection from the NYU and Mayo cohorts.

Mayo cohort: We have completed selecting of cases and controls (n=200/200) within the Mayo prostate cancer cohort from 9989 prostate cancer patients who were treated by radical prostatectomy. All cases were confirmed from pathology records. Exclusion criteria were applied as planned: (1) recurrent patients who underwent hormonal or radiation treatment before radical prostatectomy and (2) recurrent cases due to residual tumor cells after radical prostatectomy).

NYU cohort: We have completed selecting of cases and controls (n=200/200) within the NYU prostate cancer cohort in 2200 prostate cancer patients who were treated by radical prostatectomy. We applied the same inclusion and exclusion criteria as above.

2. Assembled consortium database.

We have assembled the consortium database including 400 with PSA recurrence and 400 without PSA recurrence, as we planned. The database is physically located at NYU. Selected characteristics of the study participants by recurrence status are presented in the table 1.

Table 1. Selected characteristics of study participants

	Recurrent cases (N=400)		Non-recurrent controls (N=400)
Characteristics	Systemic progression (N=200)	Non-systemic progression (N=200)	
Median age at prostatectomy	67	67	67
Tumor Stages 3 or 4, %	42.3%	25.4%	34.6%
Gleason Sum 7+	36%	53%	55%
Cohort			
NYU	100	100	200
Mayo	100	100	200

Task 2. **Pathology Review and tissue biospecimen shipping (Months 3-4):**

Pathology review (Month 3)
Shipping tissue biospecimen from the NYU to the Mayo lab (Month 4)

Mayo Cohort: Pathology review from Mayo samples was completed. Briefly, tumor blocks were characterized by pathologists with a standardized protocol. Foci highly enriched for prostate cancer (>90%) were identified by microscopic examination. Four freshly cut 10 um sections of FFPE tissue was deparaffinized and the Gleason dominant cancer focus was macrodissected.

NYU cohort: We are obtaining prostate section specimens from the Tissue Procurement Core at NYU. We have an unexpected delay due to material transfer agreements and delays in pulling of samples. However we expect to resolve this within 2-3 months.

Task 3. **RNA extraction (Months 5):**

RNA extraction for the Mayo and NYU cohort samples (Months 5)

Mayo cohort: RNA was extracted using the High Pure RNA Paraffin Kit from Roche (Indianapolis, IN). RNA was quantified using ND-1000 spectrophotometer from NanoDrop Technologies (Wilmington, DE).

NYU cohort: As soon as the MTA is approved and samples are processed, we will send samples to the Mayo for DASL assay of the NYU and MCC cohort samples.

Task 4. **DASL Assay (Months 6-12):**

DASL Assay for pre-study sample run (n=12; Months 6).
DASL Assay for study sample run (n=400 subjects; Months 7-17)

Mayo cohort: DASL expression assay (Illumina Inc, San Diego, CA) is being performed using 50 ng of cDNA according to manufacturer's instructions. DASL Assay for pre-study sample run (n=12) was completed.

DASL assay for full Mayo study samples is on-going, as we planned.

NYU cohort: As soon as the MTA is approved and samples are processed, we will send samples to the Mayo for DASL assay of the NYU samples.

RESEARCH ACCOMPLISHMENTS

- Completed nested case control selection from the NYU and Mayo cohorts.
- Constructed the consortium database.
- Completed Pathology Review and RNA extraction from Mayo samples.
- Completed DASL Assay for pre-study sample run from Mayo samples.
- DASL Assay ongoing for study sample run from Mayo samples.
- Gave an invited talk based on this project.

REPORTABLE OUTCOMES

a. Invited Seminar Presentations/Oral Presentations: The analyses results as well as the concepts of the project have been presented at the following seminar.

1. **Ahn J**, "Genes and Prostate Cancer Progression", Grand Rounds, Roswell Park Cancer Center, Buffalo, June, 2010

CONCLUSION:

We aim to examine the association of genome-wide mRNA transcription profiles in prostate tumor tissue with PSA recurrence and systemic progression (metastasis), in a consortium study based on Mayo and NYU prostate cancer cohorts. We have completed research steps as planned in Mayo cohort, but we have a 5-6 month unexpected delay in NYU samples. PI (Ahn) gave an invited talk at a cancer center based on the concept of this study under the DOD funding.

REFERENCES:
SUPPORTING DATA: None
APPENDICES: None